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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,181	11/10/1999	Snezna Rogelj	UNME-0054-1	7645

28156 7590 09/16/2004

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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,181	ROGELJ ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,8,11-19,27 and 34-38* is/are pending in the application.

4a) Of the above claim(s) *12-19,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6, 8,11,27 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the amendment filed 7/6/04, claims 2, 4 and 8 have been amended, claims 7, 9, 10, 20 cancelled, and claims 36-38 added. Claims 2-6, 8, 11-19, 27, 34-38 are now pending.

Claim 27 is now rejoined with the elected group. Claims 12-19, 34, 35 remain withdrawn from consideration. Claims 2-6, 8, 11, 27 and 36-38 are examined in this Office action.

Applicants' arguments filed 7/6/04 have been considered and found persuasive in part.

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 27, 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification asserts (e.g., page 1, lines 12-14) that the claimed compounds are effective to inhibit PDI, and to induce shedding of L-selectin from leukocytes. On page 4, it is asserted that figure 4 provides evidence that the compound designated PAODMPS* is

effective to induce L-selectin shedding from unspecified cells. The compound PAODMPS* is the product of reaction between 2, 3-dimercapto propanesulfonic acid and phenylarsine oxide, the structure of which is provided on page 25 of the specification. In addition, figure 3 shows that when the compound designated PAO* [*para*-N-(ethane-2-sulfonic acid)amino phenylarsenoxide] was contacted with neutrophils, the result was that less L-selectin could be detected in an unspecified assay. The fact that less L-selectin could be detected in an unspecified assay could be interpreted to mean either that PAO* is effective to promote L-selectin shedding or that PAO* is effective to inhibit L-selectin shedding. It is expected that applicants will assert that the result of figure 3 should be interpreted to mean that *para*-N-(ethane-2-sulfonic acid)amino phenylarsenoxide is effective to promote L-selectin shedding from neutrophils. The point is, however, that regardless of what results may have been obtained for the compound designated PAODMPS*, or for *para*-N-(ethane-2-sulfonic acid)amino phenylarsenoxide, neither of these two compounds falls within the scope of the genera recited in the cited claims. The fact that there may exist other compounds, falling outside the scope of the claimed invention, that exhibit a particular activity does not mean that the claimed compounds will promote L-selectin shedding, or that the claimed compounds will inhibit PDI. The skilled artisan cannot "predict" which compounds will promote L-selectin shedding merely by viewing its structure. Consider, for example, the following references:

- Bennett T. A. (*Journal of Immunology (Baltimore, Md. : 1950)* **156** (9) 3093-7, 1996) discloses that the compound ((N-(D,L- [2- (hydroxyaminocarbonyl)-methyl]- 4- methylpentanoyl)- L- 3- (tert- butyl)- alanyl-l -alanine, 2-aminoethyl amide) fails to promote L-selectin shedding.

- Borland, G. (*Journal of Biological Chemistry* **274** (5) 2810-5, 1999) discloses that compounds designated Ro 31-9790 and KD-IX-73-4 fail to promote L-selectin shedding, and that TIMP-3 also fails to promote L-selectin shedding. [The compounds designated Ro 31-9790 and KD-IX-73-4 are hydroxamic acid-based inhibitors of metalloproteinases]

- Solito, Egle (*FASEB journal : official publication of the Federation of American Societies for Experimental Biology* **17** (11) 1544-6, 2003) discloses (e.g., page 1544, col 2) that the receptor antagonist Boc1 fails to promote L-selectin shedding, and that the calcium entry blocker SKF-96365 similarly fails in this regard.

- Asimakopoulos G. (*Perfusion* **15** (6) 495-9, 2000) discloses that aprotinin fails to promote L-selectin shedding,

- Spoelstra F. M. (*American journal of respiratory and critical care medicine*, **162** (4 Pt 1) 1229-34, 2000) discloses that the compounds budesonide and formoterol both fail to promote L-selectin shedding.

- Recchioni R. (*Biochemical and biophysical research communications* **252** (1) 20-24, 1998) discloses that melatonin fails to promote L-selectin shedding.

- Hafezi-Moghadam A (*Journal of Experimental Medicine* **193** (7) 863-72, 2001) discloses that the compounds dexamethasone and morphine both fail to promote L-selectin shedding.

- Davenpeck K. L. (*Journal of immunology* (Baltimore, Md. : 1950), **165** (5) 2764-72, 2000) discloses (e.g., figure 4) that each of the following compounds failed to promote L-selectin shedding: EDTA, phenanthroline, batimastat, and marimastat

- Alexander S. R. (*Journal of Leukocyte Biology* **67** (3) 415-22, 2000) discloses that the protein kinase C inhibitor staurosporine failed to promote L-selectin shedding.

Thus, one cannot predict, merely by viewing a structure, which compounds will inhibit L-selectin shedding, which compounds will promote L-selectin shedding, and which will do neither.

But suppose, at some point in the future, that applicants were able to show that the compounds of the cited claims are effective to promote L-selectin shedding. The next question will be, can the skilled artisan "predict" that PDI will be inhibited? In reality, the "state of the art" in May of 1997 was such that there was no reason to expect any correlation between the propensity of a compound to promote L-selectin shedding, and its propensity to inhibit PDI.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Thus, (a) it remains to be determined whether there exists a biological assay such that the compounds of the cited claims will exhibit a positive (or negative) result; (b) it remains to be determined whether the compounds of the cited claims can promote L-selectin shedding from neutrophils, or any other cells, for that matter; (c) even if it turns out that the

compounds of claims 8 and 37 can promote L-selectin shedding from neutrophils, the reality is that one cannot "predict" whether such compounds will inhibit PDI.

Accordingly, "undue experimentation" will be required to practice the claimed invention.

✧

Claims 2-6, 8, 11, 27 and 36-38 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 2 recites the following (line 1 of the claim):

  "A compound having the **having the**".

  This contains an obvious typographical error. See also claim 36.

- Claim 3 recites the term "$S0_3$". The "O" in "$S0_3$" should be a capital "O", rather than a zero. The same error appears in other claims, such as claims 4–7.

- Claim 36 mandates that whichever of R or R' that is not hydrogen must contain at least one carbon atom and must also contain an SO_3^- group. Claim 37, on the other hand, can be interpreted to mean that either of R or R' can be just an alkyl group, without the sulfonate bonded thereto. Accordingly, the claim dependence is improper.

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. §102(b) as being anticipated by Ostromislensky (U.S.P. 1,607,299).

Ostromislensky discloses (col 2, line 22+) a compound designated "II". This is a phenylarsenious acid rather than a phenylarsenoxide. The issue here is what is meant by the term "having". This term has the effect of being "open ended" language; as such, bonding of two additional hydroxyl groups to the arsenic atom would be encompassed.

Thus, the claim is anticipated.

✧

Claim 8 is rejected under 35 U.S.C. §102(b) as being anticipated by Doak, George (*Journal of the American Chemical Society* **62**, 3010-11, 1940).

Doak discloses (table I) the following phenylarsenoxide (*para-* substitution):

$(CH_3)_2N\text{-}C_6H_4\text{-}As{=}O$

This anticipates the claims when R and R' are both methyl, and R" is hydrogen.

✧

Claim 37 is rejected under 35 U.S.C. §102(b) as being anticipated by Doak, George (*Journal of the American Chemical Society* **62**, 3010-11, 1940).

Doak discloses (table I) the following phenylarsenoxide (*para-* substitution):

$(CH_3)_2N\text{-}C_6H_4\text{-}As{=}O$

This anticipates the claims when R and R' are both methyl.

The issue here is one of claim interpretation. No doubt applicants will argue that the limitations of claim 36 must be read into claim 37. Consider, however, the following simplistic example:

100. *An apple.*

101. *The apple according to claim 100 which is an orange.*

As applicants no doubt recognize, an apple cannot be transformed into an orange merely because of a given claim dependence. Similarly, an alkyl group is not transformed into an alkylsulfonic acid group (or *vice versa*) merely because of an asserted claim dependence. If applicants do not wish to have claim 37 interpreted to mean that R or R' can be just alkyl, it is suggested that claim 37 be amended to eliminate this possibility.

Thus, the claim is anticipated.

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be

negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 2 is rejected under 35 U.S.C. §103 as being unpatentable over Eagle, Harry (*J. Pharmacol. Exp. Ther.* **70**, 221-7, 1940).

As indicated previously, Eagle discloses (table I, page 222) the following compound (*para*-substitution):

$$HOOC\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}NH\text{-}C_6H_4\text{-}As{=}O$$

Were it not for the proviso, claim 2 would be anticipated if the substituent variables could be as follows:

R is hydrogen

R' is charged ligand containing four carbon atoms, specifically the following substituent: $-CO\text{-}CH_2\text{-}CH_2\text{-}COOH$

Applicants have now excluded the possibility that R' can be a charged ligand containing four

carbon atoms. However, both of the following are close structural homologs, or "obvious variants" of the R' group disclosed in the reference:

$-CO-CH_2-COOH$

$-CO-CH_2-CH_2-CH_2-COOH$

The medicinal chemist of ordinary skill would have expected, *a priori*, substantially identical activity for the two homologs. [*In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544)].

Thus, the claim is rendered obvious.

✺

It is suggested that applicants delete reference to PAO in claim 14, or else that a claim be added which is the same as claim 14, but without reference to PAO. In addition, claim 14 should be dependent on a pending claim (e.g., claim 2), rather than a cancelled claim (e.g., claim 1). Rejoining of method claims is not required if the method claim is drawn to a compound which is not encompassed by the claims that are drawn to compounds *per se*. In a similar vein, it is suggested that claim 19 be written in independent form, so that it is clear that use of a compound of claim 2 or 8 is unequivocally mandated. At present, claim 19 could be interpreted to mean that the assay can be conducted using compounds other than those recited in claim 2 or 8. Similarly, it is suggested that claims 16-18 be cancelled, since these claims clearly do not require the use of any of the claimed compounds. It is also suggested that claim 12 be made dependent on a pending claim (e.g., claim 2), rather than a cancelled claim (e.g., claim 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800